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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/889,317	07/13/2001	Ralph A. Tripp	6395-59041	2319

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KLARQUIST SPARKMAN, LLP
121 S.W. SALMON STREET
SUITE 1600
PORTLAND, OR 97204

EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/889,317	TRIPP ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,13,14,19-22,31,32,37,38,41 and 42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,13,14,19-22,31,32,37,38,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a rule 371 continuation of PCT Serial Number PCT/US00/01032, which claims the benefit of the filing date of provisional application 60/116,835.

Claims 5-12, 15-18, 23-30, 33-36, 39-40 and 43-44 have been canceled.

Claims 1-4, 13, 14, 19-22, 31, 32, 37, 38 and 41-42 are currently pending and are the subject of examination in the present Office Action.

1. In view of Applicant's amendment filed August 8, 2005, no outstanding ground of rejection is maintained. The following grounds of rejection have been necessitated by Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

2. Claims 1-3, 13, 14, 19, 21, 31, 32, 37, 38, 41, and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudlacz et al (Eur. J. Pharmacol. [1994] 270:291-300; U on form PTO-892 mailed 9/22/2004) in view of Jafarian et al (Life Sciences [1995] 57(2):143-153; V on form PTO-892 mailed 9/22/2004), Hemmingsson et al (Scand. J. Infect. Dis. [1993] 25(6):783-985; U on form PTO-892 mailed herewith), Moneret-Vautrin et al (Rhinology [1992] 30(3):161-168; V on form PTO-892 mailed herewith) and U.S. Patent No. 5,256,766 to Coughlin (A on form PTO-892 mailed 9/22/2004).

The claims read upon the treatment of viral infections with anti-substance P antibodies. It has long been known in the art that severe viral respiratory infections cause inflammation and airway

hyperresponsiveness, as such severe infections are commonly treated with anti-inflammatory medicaments to treat the symptoms of inflammation in the respiratory tract.

Kudlacz teaches that parainfluenza virus infection of the respiratory tract results in substance P release, hyperresponsiveness and inflammation (see entire document, Abstract, paragraph bridging pages 291-292 and page 298, column 2 in particular). Kudlacz further teaches that in conditions associated with inflammation, such as asthma, tissue substance P levels have been shown to be reduced and levels in local fluids are increased, suggesting release of substance P at the inflammatory focus (paragraph bridging pages 291-292 in particular) and the direct involvement of substance P in inflammation and hyperresponsiveness.

Jafarian teaches that administration of rat monoclonal anti-substance P antibody in a guinea-pig model of asthma "prevents" substance P-induced bronchospams (Abstract in particular). Jafarian teaches the administration of anti-substance P antibodies 30 minutes prior to the administration of exogenous substance P to the animals in a model of asthma. Jafarian further teaches the use and effectiveness of a rat monoclonal antibody.

The combined references do not teach nasal administration of antibodies.

Moneret-Vautrin teaches that substance P is released into the nasal mucosa upon irritation of the nasal epithelium, resulting in eosinophilia and inflammation (Abstract in particular). Hemmingsson teaches the administration of antibodies intranasally to human subjects significantly reduces the incidence of upper respiratory tract infection. Hemmingsson teaches that nasal administration of antibody is an effective prophylactic treatment for infection (Abstract in particular).

The combined references do not teach antibody fragments, including $F(ab')_2$.

The '766 patent teaches that the use of immunologically reactive fragments of polyclonal or monoclonal antibodies, such as the Fab, Fab', or $F(ab')_2$ fragments is preferable in a therapeutic context because these fragments are generally less immunogenic than the whole immunoglobulin (column 12, lines 8-17 in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of Kudlacz and Jafarian to treat viral induced airway inflammation and hyperresponsiveness by administration of anti-substance P antibodies. One would have been motivated to combine the teachings with a reasonable expectation of success by the teachings of Kudlacz that viral infection of the lung results in hyperresponsiveness and inflammation related to substance P levels and the teachings of Jafarian that antibody to substance P is effective in treating and preventing inflammation and hyperresponsiveness in the respiratory tract.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to apply the anti-substance P directly to the nasal mucosa of a subject. The artisan would have been motivated to make this further combination, with a reasonable expectation of success, by the teachings of Moneret-Vautrin that nasal insults result in the release of substance P into the nasal mucosa and the teachings of Hemmingsson that antibodies directly applied to the nasal mucosa are effective in binding and neutralizing their target antigen. The artisan would reasonably expect, therefore, that such application would be effective in reducing the inflammatory response in the nasal mucosa to an infection.

Further, it would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to substitute antibody fragments for the intact anti-substance P antibodies taught by Jafarian. One would have been motivated to combine the teachings with a reasonable expectation of success by the well-known principle in the art, as demonstrated by the '766 patent, that antibody fragments are less immunogenic than whole molecule antibodies and are therefore better tolerated by the subject.

Claims 13, 14, 31 and 32 are included because, while the references do not specifically teach a daily dosage of antibody within the recited range, silence about a particular property does not necessarily constitute its absence and dosages of medicaments are determinable by routine experimentation by the artisan.

Claims 41 and 42 are included because, while Kudlacz and Jafarian are silent about reduction of levels of intracellular cytokines including IL-2, IL-4, IL-6 or IFNγ, silence about a particular property does not constitute its absence. The method of treatment is the same and application of anti-Substance P antibodies for reducing inflammation will also reduce the levels of inflammatory cytokines. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that there is a difference between the materials, i.e., that the claims are directed to new materials and that such a difference would have been considered unexpected by one of ordinary skill in the art, that is, the claimed subject matter, if new, is unobvious. In the absence of evidence to the contrary, the burden is on the Applicant to prove that the claimed materials are different from those taught by the prior art and to establish patentable differences. See *In re* Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte* Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

3. Claims 4, 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudlacz et al (Eur. J. Pharmacol. [1994] 270:291-300; U on form PTO-892 mailed 9/22/2004) in view of Jafarian et al

(Life Sciences [1995] 57(2):143-153; V on form PTO-892 mailed 9/22/2004), Hemmingsson et al (Scand. J. Infect. Dis. [1993] 25(6):783-985; U on form PTO-892 mailed herewith), Moneret-Vautrin et al (Rhinology [1992] 30(3):161-168; V on form PTO-892 mailed herewith) and U.S. Patent No. 5,256,766 to Coughlin (A on form PTO-892 mailed 9/22/2004) as applied to claims 1, 3 and 19 above, and further in view of Larsen (Clin. Resp. Physiol. [1986] 22(suppl. 7):35-37; W on form PTO-892 mailed 9/22/2004).

Kudlacz, Jafarian, Moneret-Vautrin, Hemmingsson and the '766 patent have been discussed supra.

The combined references do not teach respiratory syncytial virus.

Larsen teaches that 'insults' to the bronchial airways result in inflammation and hyperresponsiveness. Larsen teaches that such insults include infection of the airway by respiratory syncytial virus (Abstract in particular).

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to combine the teachings of the references to treat substance P mediated inflammatory responses to respiratory syncytial virus. One would have been motivated to combine the teachings with a reasonable expectation of success by the teachings of Kudlacz that viral infection of the lung results in hyperresponsiveness and inflammation related to substance P levels and the teachings of Larsen that respiratory syncytial virus infection of the bronchial airways causes inflammation and hyperresponsiveness. One would have been further motivated to treat viral inflammation in the respiratory tract with anti-substance P antibodies by the teachings of Jafarian that antibody to substance P is effective in treating and preventing inflammation and hyperresponsiveness in the respiratory tract.

Conclusion

4. No claim is allowed.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
November 22, 2005

David a Saunders
DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT 182 1644